REMARKS/ARGUMENTS

Upon entry of the amendment of October 3, 2006, Claims 54, 55 and 57 are pending in this application.

Advisory Action of October 24, 2006

According to the Advisory Action mailed on October 24, 2006, the claim amendments and arguments submitted on October 3, 2006 did not place the application in condition for allowance since *"besides the speculative statement at the end of Example 9 of the specification, [there are] no actual data showing that PRO362 polynucleotide is more highly expressed in inflammatory disease compared to normal healthy control subject. In addition, there is no further supporting evidence to indicate that the claimed polypeptide encoded by the polynucleotide is also differentially expressed in the inflammatory disease when compared to healthy control for one skilled in the art to use it as a diagnostic marker."* From this, the Examiner concludes that the *"specification provides a mere invitation to experiment,"* and does not provide a readily available utility. In addition, claims 54-55 and 57 were rejected under 35 U.S.C. 112, first paragraph, stating that *"since the claimed invention is not supported by either a specific and/or substantial asserter utility or a well established utility . . . , one skilled in the art clearly would not know how to use the claimed invention so that is would operate as intended without undue experimentation."*

Rejection under 35 U.S.C. 101 - Utility

Applicants rely on the usefulness of the anti-PRO362 polypeptides claimed in the present application in the diagnosis of inflammatory diseases in mammals to comply with the requirements of 35 U.S.C. 101. This utility is specifically disclosed, for example, at page 3, lines 31-40 of the specification.

Throughout the specification, Applicants teach the involvement of PRO362 in inflammation. While some of this teaching, like the teaching at page 42, lines 24-32 and in Example 9, may be based on homology to the known JAM protein, this reason in and by itself is not sufficient to discount the diagnostic utility of PRO362. It is well established that the

patentability of an invention does not depend on the manner by which the invention was made. Indeed, according to the Examination Guidelines for the Utility Requirement (MPEP 2107), "If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." Absent evidence to the contrary, the asserted diagnostic utility should be accepted as credible.

In order to address the Examiner's comments concerning to alleged lack of evidence that that the PRO362 polypeptide is overexpressed in inflammatory diseases relative to non-diseased control, enclosed is a Declaration by Dr. Menno van Lookeren Campagne, including experimental results supporting the diagnostic utility of the polypeptide claimed in the present application.

In paragraphs 5-8 of the Declaration, Dr. van Lookeren describes the protocols of in situ hybridization and immunohistochemical staining experiments examining the expression of PRO362 mRNA in a wide variety of tissues, including normal and inflamed tissues.

Following discussion of the results of in situ hybridization experiments in paragraph 9, in paragraph 10 of the Declaration Dr. Van Lookeren provides data showing that PRO362 mRNA levels in synovial cells obtained from a patient with osteoarthritis were significantly elevated relative to normal synovial cells.

In order to quantitatively determine PRO362 mRNA expression leveld in inflammatory bowel disease (IBD), PRO362 mRNA was extracted from colon tissue from patients with ulcerative colitis, Crohn's diseases and from patients with no manifestation of IBD, and real-tipe PCR was performed to measure relative expression levels. As discussed in paragraph 11 of the Declartion, expression levels of PRO362 mRNA were significantly higher in patients with IBD than in patients with no manifestation of IBD. Similarly, PRO362 mRNA levels were significantly increased in the lung tissue of patients with COPD and asthma, over the levels in normal patients without the disease.

In paragraph 12 of his Declaration, Dr. Van Lookeren described immunohistochemistry experiments showing the expression of PRO362 protein in various tissues.

In paragraph 13, the Declaration shows hat PRO362 protein was expressed in a subset of synovial cells and in tissue macrophages in the synovium of a patient with rheumatoid arthritis, while expression was not detected in control synovium obtained from a normal patient.

Paragraph 14 of the Declaration provides data showing PRO362 expression is atherosclerotic plaques.

Based on these experimental data, which show that PRO362 mRNA and protein expression correlates with a variety of inflammatory diseases, and his many years of scientific experience in the pertinent field, Dr. van Lookeren confirms that PRO362 is a good target for the diagnosis of inflammatory disease, and that such diagnosis can be carried out, for example, using anti-PRO362 antibodies (paragraph 15 of the Declaration).

In view of the foregoing arguments, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Rejection under 35 U.S.C. 112, first paragraph - Enablement

Claims 54, 55 and 57 were rejected under 35 U.S.C. 112, first paragraph "since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility" for the reasons set forth in the utility rejection, "one skilled in the art clearly would not know how to use the claimed invention s that it would operate as intended without undue experimentation."

In response to the lack of utility rejection, Applicants have shown that the claimed invention is supported by a specific and substantial asserted diagnostic utility. Accordingly, one of ordinary skill would clearly know how to use the claimed invention without undue experimentation, and the present rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-1216 R1C1D1**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

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